Office Action Summary	Application No.	Applicant(s)
	10/563,042	ANAND ET AL.
	Examiner	Art Unit
	TREVOR LOVE	1611

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-10* is/are pending in the application.

4a) Of the above claim(s) *10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/14/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/14/2011 has been entered.

Claims 1-4 and 6-10 are pending.

Claims 5 and 11-51 are cancelled.

Claim 10 remains withdrawn.

Claims 1-4 and 6-9 are currently under consideration.

No claims are currently amended.

Withdrawn Rejections

The rejection of claim 5 under 35 U.S.C. 103(a) as being unpatentable over Sen et al as evidenced by Entrez Gene in view of Patel et al and Hauf et al (IDS reference) is withdrawn in view of Applicant's cancellation of said claim.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sen et al (Oncogene) as evidenced by Entrez Gene (AURKA Aurora Kinase A) in view of Patel et al (Oncogene) and Hauf et al (Journal of Cell Biology) (IDS reference).

Sen teaches that human breast cancer exhibits an amplified and overexpressed amount of BTAK which is a serine/threonine kinase (see entire document, for instance,

Title). Entrez Gene evidences that BTAK is also known as aurora kinase A (see entire document, for instance section labeled "Summary").

Sen fails to directly teach treating breast cancer with an Aurora A Kinase inhibitor, namely Hesperadin, or with a mitotic spindle assembly inhibitor, namely paclitaxel.

Patel teaches that paclitaxel is a microtubule-stabilizing agent, wherein cells exit mitosis aberrantly and fractionate into hypodiploid populations during cell cycle analysis (see entire document, for instance, page 4163, first column, first paragraph). Patel further teaches that breast cancer cells are sensitive to paclitaxel (see entire document, for instance, Title).

Hauf teaches that Hesperadin is an aurora A kinase inhibitor (see entire document, for instance page 284, column 2, last paragraph). Hauf proffers that Hesperadin treatment turned off checkpoint signaling in Taxol-treated cells because all kinetochores progressively accumulated stably attached microtubles. Hauf teaches that Hesperadin might allow cells treated with paclitaxel to exit the mitotic phase by stabilizing improper microtubule attachments (see entire document, for instance page 288, column 2, last sentence).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the antineoplastic agent paclitaxel of Patel and the aurora A kinase inhibitor Hesperadin of Hauf to treat a patient with breast cancer, such as those of Sen. One would have been motivated to do so since both the paclitaxel of Patel and the Hesperadin of Hauf are directed to stabilizing microtubule attachment and

exiting cells from mitosis wherein the exiting cell is in an aberrant or improper condition. Also, one would have been motivated to utilize the paclitaxel of Patel to treat the breast cancer of Sen since Patel teaches that breast cancer cells are sensitive to paclitaxel. There would be a reasonable expectation of success since both Sen and Patel are directly drawn to breast cancer, and Sen identifies a clear nexus between aurora A kinase and breast cancer.

Response to Arguments

Applicant argues in the remarks filed 07/14/2011 that "Hauf teaches that Hesperadin is an Aurora B kinase inhibitor" (see remarks, page 5, emphasis original). Applicant proceeds on pages 5 and 6 of the remarks to indicate a plurality of locations where Hauf states that Hesperadin is an Aurora B kinase inhibitor. Applicant's argument is not found persuasive since Hauf clearly identifies that Hesperadin inhibits Aurora A. While Hauf does indicate that this effect is not as extensive as the inhibition of Aurora B, the inhibition can be seen in Figure 3A as well as in Hauf's identification that at least to some extent Hesperadin is an Aurora A inhibitor (see Hauf, entire document, for instance, Figure 3A and page 284, column 2, last paragraph). It is further noted that the paxlitaxol of Patel and the Hesperadin of Hauf are taught as being useful for the same purpose, namely stabilizing microtubule attachment and exiting cells from mitosis wherein the exiting cell is in an aberrant or improper condition. Therefore, one would have been motivated to utilize the Hesperadin of Hauf in addition to the paxlitaxol of Patel since it is known to combine two components for the same purpose in order to arrive at a third composition for the exact same purpose. It is noted that MPEP 2144.05

states: ""It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992).

Applicant further argues that Applicant has previously antedated the Hauf reference by reference to Anand. This argument has previously been addressed in the Non-Final Rejection mailed 06/11/2010. However, for completeness, it is again noted that Applicant has failed to antedate the Hauf reference. Applicant's argument and previously filed declaration are not found persuasive since it is clear that Applicant has not met the requirements clearly set forth in MPEP 715 for antedating a reference. *For instance*, Applicant has failed to provide a clear showing wherein the "showing of facts shall be such, in character and weight, as to establish reduction to practice prior to the effective date of the reference, or conception of the invention prior to the effective date of the reference coupled with due diligence from prior to said date to a subsequent reduction to practice or to the filing of the application. Original exhibits of drawings or records, or photocopies thereof, must accompany and form part of the affidavit or declaration or their absence must be satisfactorily explained." The Anand reference fails to identify that Applicant had possession of the full scope of the invention, for instance, the Anand reference does not even name a single Aurora A kinase inhibitor

(such as Hesperadin). Further, Applicant has not provided any showing of diligence from said date or a reduction to practice as of said date. Therefore, Applicant's arguments and declaration are not found persuasive to antedate the Hauf reference.

Applicant further argues that Hauf teaches away from the claimed invention (see remarks, page 8). Applicant's argument is not found persuasive since first, Taxol is identified in Patel as "a microtubule-stabilizing agent", wherein the addition of Hesperadin would increase said effect and cause the cells to exit mitosis, and therefore the breast cancer cells would not continue dividing or growing (see Hauf page 282, 2nd column). Further, while hesperadin overrides Taxol, Hauf does not show that this override causes the cell to proceed through mitosis and continue to grow, rather, Hauf teaches that hesperadin allows the cells to proceed from metaphase to anaphase (e.g., hesperadin overrides the checkpoint arrest by taxol), however the stabilization of improper microtubule attachments causes these cells to exit mitosis early without cytokinesis resulting in massive polyploidy and, while the cells are able to grow, they do not proliferate (see Hauf page 282, 2nd column). Second it is noted that while a reasonable expectation is required, absolute predictability is not. It is noted that MPEP 2143.02 states "[o]bviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976)".

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sen et al (Oncogene) as evidenced by Entrez Gene (AURKA Aurora Kinase A) in view of Patel et al (Oncogene) and Hauf et al (Journal of Cell Biology) (IDS reference) as applied to claims 1-4 and 8-9 above, and further in view of Slamon et al (N.E.J.M.).

The teachings of Sen, Patel, and Hauf are set forth above.

Sen fails to directly teach the presence of an antibody which is an aurora A kinase inhibitor.

Slamon teaches that recombinant monoclonal antibody are useful in breast cancer patients to aid in correcting the over expression of HER2 which is over-expressed in 25 to 30% of breast cancers (see Abstract, first eight lines).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize antibodies to mediate the over-expression of aurora A kinase in the breast cancer patients of Sen. One would have been motivated to do so since Slamon teaches the mediation of HER2 over-expression in breast cancer patients by the utilization of antibodies. There would be a reasonable expectation of success in the combination since Applicant identified in the instant specification that there are many well known methods of acquiring antibodies (see instant specification, page 7, lines 1-13). Furthermore, Sen teaches that aurora A kinase is over-expressed in breast cancer patients, and Slamon teaches that antibodies can be used to mediate over-expression of HER2. One would have looked to various options to overcome the aurora A kinase over-expression, such as antibodies. One would have particularly looked to

antibodies since Slamon teaches a method of reducing HER2 gene over-expression by using antibodies (see Slamon (see page 783, last paragraph through 784, first paragraph).

Response to Arguments

Applicant argues in the remarks filed 07/14/2011 that Slamon fails to cure the deficiencies alleged above in Hauf. Applicant's arguments are not found persuasive. See above response to arguments.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sen et al (Oncogene) as evidenced by Entrez Gene (AURKA Aurora Kinase A) in view of Patel et al (Oncogene) and Hauf et al (Journal of Cell Biology) (IDS reference) as applied to claims 1-4 and 8-9 above, and further in view of Obermiller et al (Breast Cancer Res).

The teachings of Sen, Patel, and Hauf are set forth above.

Sen fails to directly teach the presence of a sense or anti-sense nucleic acid which is an aurora A kinase inhibitor.

Obermiller teaches that gene therapy is useful when trying to correct specific molecular defects that contribute to the cause or progression of cancer, specifically, breast cancer (see abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize sense or anti-sense nucleic acids to mediate the over-expression of aurora A kinase in the breast cancer patients of Sen. One would have

been motivated to do so since Obermiller teaches that gene therapy provides the ability to correct specific molecular defects that contribute to the cause or progression of cancer, this would include the over-expression of aurora A kinase in breast cancer patients. There would be a reasonable expectation of success in the combination since Applicant identified in the instant specification that there are many well known methods of down-regulating gene expression. Specifically, the instant specification states "[T]he use of these approaches [sense and anti-sense] to down-regulate gene expression is now well-established in the art (see instant specification, page 8, lines 6-9 and page 10, lines 21-27).

Response to Arguments

Applicant argues in the remarks filed 07/14/2011 that Obermiller and Lange fail to cure the deficiencies alleged above in Hauf. Applicant's arguments are not found persuasive. See above response to arguments.

Conclusion

No claims allowed. All claims rejected. No claims objected.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued

examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TREVOR M. LOVE whose telephone number is (571)270-5259. The examiner can normally be reached on Monday-Thursday 7:30-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TL

/SHARMILA G. LANDAU/

Supervisory Patent Examiner, Art Unit 1611